NOVEL METHOD TO DIFFERENTIATE HUMAN EMBRYONIC STEM CELLS INTO DOPAMINERGIC NERVE CELLS

SUMMARY

The National Institute on Drug Abuse's Development and Plasticity Section is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate, or commercialize novel methods to differentiate human embryonic stem cells into dopaminergic nerve cells. The invention described here is a novel method of differentiating human embryonic stem cells (hESCs) into dopaminergic nerve cells, which is preferable to the currently available dopaminergic differentiation techniques.

REFERENCE NUMBER

E-176-2008

PRODUCT TYPE

- Research Materials

KEYWORDS

- Parkinson's Disease
- Neurological Diseases

COLLABORATION OPPORTUNITY

This invention is available for licensing and co-development.

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DESCRIPTION OF TECHNOLOGY

Neurodegenerative disorders encompass a range of debilitating conditions including Parkinson''s disease, Alzheimer's disease, and Huntington''s disease. The primary cause of motor dysfunction for Parkinson''s disease has been linked to degeneration of dopaminergic neurons in specific areas of the brain. Transplantation of dopaminergic neurons in affected areas of the brain in late stage Parkinson''s disease has potential clinical utility in human patients. However, fetal nigral transplantation therapy generally requires human tissue from at least 3-5 embryos to obtain a clinically reliable improvement in the patient, thus demonstrating a need for a larger and more reliable source of dopaminergic cells. Other techniques for generating dopaminergic neurons from human embryonic stem cells (hESCs) are either

inefficient, require the use of animal-derived cells or products, or involve complex and lengthy procedures.

This invention describes a novel combination of soluble proteins which, when used under appropriate cell culture conditions, causes hESCs to differentiate into dopaminergic nerve cells. This invention potentially provides a source of sufficient dopaminergic cells not only for the clinical transplantation of dopaminergic tissue, but also for in vitro studies of human cells useful for pharmaceutical screens related to neurodegenerative disorders and substance abuse.

Further R&D Needed:
For transplantation in human subjects, a great deal of additional development is needed. It would be necessary to:

- Develop a differentiation model based on the current discoveries that will comply with GMP (good manufacturing practices) regulations
- Ensure that no undifferentiated cells remain in the mixture, that the method could be applied to various lines of human embryonic stem cells, and that differentiated cells do not form tumors when transplanted into the brain. The procedure would need to be optimized for transplantation, by varying parameters such as concentrations of growth factors used.
- Determine efficacy and safety in rodent and sub-human primate transplantation models.

In contrast, cells produced using the methods described in this invention can be used as an in vitro model for drug testing without further development.

POTENTIAL COMMERCIAL APPLICATIONS

- Human dopaminergic cell source for neuronal transplantation, with potential clinical application to Parkinson''s disease and possibly other neurodegenerative disorders.
- Human dopaminergic cell source for in vitro models for pharmaceutical screens relevant to neurodegenerative disorders and substance abuse.

COMPETITIVE ADVANTAGES

- Ability to differentiate human embryonic stem cells (hESCs) into dopaminergic nerve cells with very high efficiency.
- The protocol is technically simple and rapid.
- In contrast to previous protocols, this method does not require the use of animal-derived cells or products, selection of neural precursor cells, retinoic acid or multiple treatment phases.

INVENTOR(S)

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DEVELOPMENT STAGE

- Discovery (Lead Identification)

PATENT STATUS

- **U.S. Issued:** US, 8,628,962 (14 Jan. 2014)

THERAPEUTIC AREA

- Central Nervous System, Mental and Behavioral, Pain